

510, 064

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 October 2003 (16.10.2003)

PCT

(10) International Publication Number
WO 03/084510 A1

- (51) International Patent Classification⁷: **A61K 9/20**, 31/495, 31/445
- (21) International Application Number: **PCT/IB02/01068**
- (22) International Filing Date: **4 April 2002 (04.04.2002)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (71) Applicant (*for all designated States except US*): **DR. REDDY'S LABORATORIES LTD.** [IN/IN]; Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **KAMALAKAR, Talasila** [IN/IN]; Dr. Reddy's Laboratories Ltd., Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN). **DASH, Debashis** [IN/IN]; Dr. Reddy's Laboratories Ltd., Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN). **SRINIVAS, Irukula** [IN/IN]; Dr. Reddy's Laboratories Ltd., Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN). **DHANORKAR, Vipin, Tatyasaheb** [IN/IN]; Dr. Reddy's Laboratories Ltd., Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN). **MOHAN, Mailatur, Sivaraman** [IN/IN]; Dr. Reddy's Laboratories Ltd., Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN).
- (74) Common Representative: **DR. REDDY'S LABORATORIES LTD.**; Post Box No.15, Kukatpally, Hyderabad 500 072, Andhra Pradesh (IN).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Declaration under Rule 4.17:**
— *of inventorship (Rule 4.17(iv)) for US only*
- Published:**
— *with international search report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **NOVEL PHARMACEUTICAL COMPOSITIONS FOR ANTIHISTAMINIC-DECONGESTANT COMBINATION AND METHOD OF MAKING SUCH COMPOSITIONS**

(57) Abstract: The present invention relates to pharmaceutical compositions of antihistamine-decongestant combination. Specifically the invention relates to bilayered tablet formulation comprising antihistaminic decongestant combination. More specifically present invention relates to the novel polymorph of fexofenadine or pharmaceutically accepted salts thereof, with at least one decongestant in the form of bilayered tablet. The preferred polymorphs are polymorph A and polymorph X of fexofenadine hydrochloride.



WO 03/084510 A1

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01068

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/20 A61K31/495 A61K31/445

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | US 6 267 986 B1 (JAIN GIRISH KUMAR ET AL) 31 July 2001 (2001-07-31) cited in the application column 2, line 44 - line 61 column 5 -column 10; examples --- | 1,9,14, 16,17 |
| X | US 4 996 061 A (WEBB NORVAL E ET AL) 26 February 1991 (1991-02-26) cited in the application column 1, line 29 - line 48 column 3, line 52 -column 4, line 40 examples column 7, line 33 - line 41 claims --- -/- | 1,14,16, 17 |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the International search

14 November 2002

Date of mailing of the International search report

25/11/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Rankin, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01068

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>WO 99 09957 A (HOECHST MARION ROUSSEL INC) 4 March 1999 (1999-03-04) page 3, line 14 - line 26 page 19; example 1 page 24; tables 2,3 page 30; tables 4,5 claims</p> <p>---</p> | 1,5,14, 16,17 |
| X | <p>US 6 039 974 A (LEFLER JOHN R ET AL) 21 March 2000 (2000-03-21) column 2, line 52 -column 3, line 17 column 9, line 58 -column 10, line 17 column 15, line 12 - line 55 examples; tables column 16, line 30 -column 18, line 44</p> <p>---</p> | 1,5, 14-17 |
| X | <p>WO 01 85148 A (RANDALL DOUGLAS E ;AVENTIS PHARMA INC (US); NICHOLAS JAMES M (US)) 15 November 2001 (2001-11-15) page 1, line 10 - line 19 page 6 page 8, line 3 -page 10, line 20 claims 38-49</p> <p>---</p> | 1,5, 14-17 |
| A | <p>WO 01 94313 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); DAVIES JULIAN ANTH) 13 December 2001 (2001-12-13) page 1, line 1 - line 10 page 3 -page 5 page 7; example 1 figures</p> <p>---</p> | 1-17 |
| A | <p>SIMPSON K ET AL: "FEXOFENADINE A REVIEW OF ITS USE IN THE MANAGEMENT OF SEASONAL ALLERGIC RHINITIS AND CHRONIC IDIOPATHIC URTICARIA" DRUGS, ADIS INTERNATIONAL LTD, AT, vol. 2, no. 59, February 2000 (2000-02), pages 301-321, XP001079065 ISSN: 0012-6667 page 310 -page 312</p> <p>---</p> | 1-17 |
| A | <p>SUSSMAN G L ET AL: "THE EFFICACY AND SAFETY OF FEXOFENADINE HCI AND PSEUDOEPHEDRINE, ALONE AND IN COMBINATION, IN SEASONAL ALLERGIC RHINITIS" JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, MOSBY - YEARLY BOOK, INC, US, vol. 104, no. 1, July 1999 (1999-07), pages 100-106, XP001055760 ISSN: 0091-6749 page 101</p> <p>---</p> | 1-17 |
| | <p>---</p> <p>---/---</p> | |

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01068

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| T | <p>WO 02 080857 A (DOLITZKY BEN-ZION ;GROSS IRWIN (IL); TEVA PHARMA (IL); WIZEL SHLOM) 17 October 2002 (2002-10-17) page 3 -page 6 page 26 -page 37; examples -----</p> | 1-17 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/01068

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 17
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 17 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 17

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern: Application No

PCT/IB 02/01068

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|----|---------------------|---|--|
| US 6267986 | B1 | 31-07-2001 | AU 7032500 A EP 1217997 A1 WO 0121168 A1 | 24-04-2001 03-07-2002 29-03-2001 |
| US 4996061 | A | 26-02-1991 | AT 79746 T AU 2345988 A CA 1314485 A1 CN 1032738 A ,B DE 3874072 D1 DE 3874072 T2 DK 559088 A EP 0311067 A1 ES 2046270 T3 FI 884545 A ,B, GR 3005542 T3 HU 48816 A2 IE 61130 B IL 87943 A JP 1128925 A JP 2722219 B2 KR 9607748 B1 NO 884443 A ,B, NZ 226482 A PH 26155 A PT 88682 A ,B ZA 8807413 A | 15-09-1992 20-04-1989 16-03-1993 10-05-1989 01-10-1992 08-04-1993 08-04-1989 12-04-1989 01-02-1994 08-04-1989 07-06-1993 28-07-1989 05-10-1994 16-02-1992 22-05-1989 04-03-1998 12-06-1996 10-04-1989 26-09-1990 18-03-1992 01-11-1988 26-07-1989 |
| WO 9909957 | A | 04-03-1999 | AU 725811 B2 AU 8582098 A BR 9812001 A CN 1268050 T EE 200000098 A EP 0998272 A1 HU 0002183 A2 JP 2002511102 T NO 20000932 A NZ 501248 A PL 337348 A1 SK 177799 A3 TR 200000517 T2 WO 9909957 A1 ZA 9807552 A | 19-10-2000 16-03-1999 26-09-2000 27-09-2000 15-12-2000 10-05-2000 28-11-2000 09-04-2002 18-04-2000 29-06-2001 14-08-2000 11-07-2000 21-08-2000 04-03-1999 26-02-1999 |
| US 6039974 | A | 21-03-2000 | NONE | |
| WO 0185148 | A | 15-11-2001 | AU 6116501 A WO 0185148 A2 US 2002022639 A1 | 20-11-2001 15-11-2001 21-02-2002 |
| WO 0194313 | A | 13-12-2001 | AU 6537701 A WO 0194313 A2 | 17-12-2001 13-12-2001 |
| WO 02080857 | A | 17-10-2002 | WO 02080857 A2 | 17-10-2002 |